Conversion of Alcohols, Thiols, and Trimethysilyl Ethers to Alkyl Cyanides Using Triphenylphosphine/ 2,3-Dichloro-5,6-dicyanobenzoquinone/*n*-Bu_4NCN

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Triphenylphosphine and 2,3-dichloro-5,6-dicyanobenzoquinone afford an adduct, which in the presence of *n*-Bu_4NCN converts alcohols, thiols, and trimethylsilyl ethers into their corresponding alkyl cyanides in good to excellent yields at room temperature. This method is highly selective for the conversion of 1° alcohols in the presence of 2° and 3° ones, thiols and silyl ethers.

Introduction

The nitrile functional group is widely recognized as a useful intermediate in organic synthesis.[1,2] Different synthetic methodologies have been reported for the introduction of this group to organic compounds.[3] In replacement of the leaving groups with cyanide ions in organic halogen compounds, aryl sulfonates, alcohols, esters, ethers, nitro or amino compounds, and diazonium salts could be used as suitable substrates for this type of reaction.[4] Among these functionalities, alkyl halides and alcohols are used more frequently for this transformation. For primary halides, the reaction is usually substitution;[4] however, with secondary and tertiary alkyl halides, competition between substitution and elimination results in low yields of nitriles. The transformation of alcohols to nitriles is an important method for the elongation of the carbon chain and is usually performed through prior conversion of the hydroxyl group to leaving groups such as halides and sullfonates. The more simplified one-pot method for the conversion of alcohols into cyanides based on the concept of the Mitsunobu reaction using HCN/PPh_3/DEAD in moderate yields is described.[5−7] The use of *n*-$Bu_3P/CCl_4/KCN$/18-crown-6[5f] for the conversion of only primary alcohols to nitriles and the modification of the Mitsunobu reaction using acetone cyanohydrin as a source of HCN are also reported.[8,9] However, this latter reaction gives low yields for hindered primary alcohols (17%) and also for secondary alcohols (10−58%).

SCHEME 1

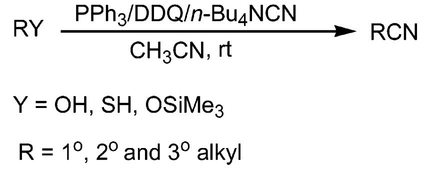

TABLE 1. Conversion of Benzyl Alcohol to Benzyl Cyanide Using *n*-Bu_4NCN in the Presence of PPh_3 and Different Reagents in Acetonitrile at Room Temperature

entry	mixed reagent	time (h)	conversion %[a]
1	PPh_3/DDQ	immediately	100
2	PPh_3/*p*-chloranil	24	7
3	PPh_3/DEAD	24	10
4	PPh_3/DEACD	24	0
5	PPh_3/TCNE	24	0
6	PPh_3/tetracyclone	24	0
7	PPh_3/PTAD	24	0

[a] GC yield using an internal standard.

In this paper, we report a novel and simple method for the efficient conversion of 1°, 2°, and 3° alcohols as well as thiols and trimethylsilyl ethers into their corresponding nitriles.

Results and Discussion

Recently, we have reported on the application of PPh_3/DDQ/R_4NX (X = Cl, Br, I) for the conversion of alcohols, thiols, and selenols into their corresponding alkyl ha-

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(4) Kornblum, N.; Smiley, R. A.; Blackwood, R. K.; Iffland, D. C. *J. Am. Chem. Soc.* **1955**, *77*, 6269.

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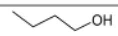
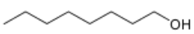
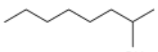
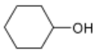
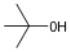
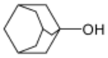
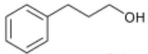
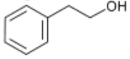
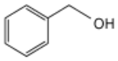
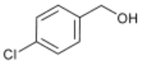
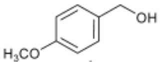
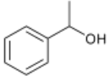
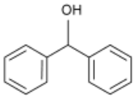
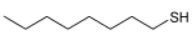
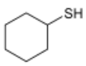
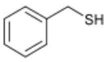
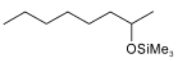
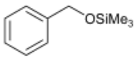
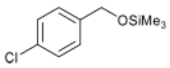
(9) Aesa, M. C.; Baan, G.; Novak, L.; Szantay, C. *Synth. Commun.* **1995**, *25*, 2575.

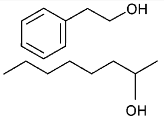
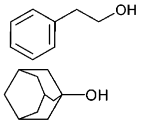
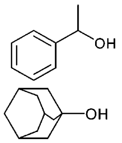
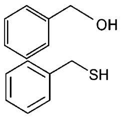
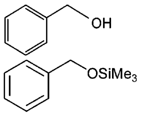
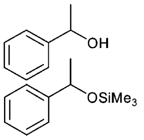
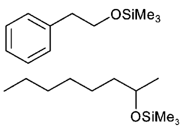
10.1021/jo035238v CCC: $27.50

TABLE 2. Conversion of Alcohols, Thiols, and Silyl Ethers into Alkyl Cyanides

Entry	ROH	Time	Conversion %[a]	Isolated yield %
1		Immediately	100	-
2		Immediately	100	92
3		5 min	100	90
4		10 min	100	83
5		24 h	50	40
6		24 h	80	72[b]
7		Immediately	100	93
8		Immediately	100	92
9		Immediately	100	94
10		Immediately	100	90
11		Immediately	100	92
12		Immediately	100	91
13		20 h	80	70
14		3 h	100	88
15		5 h	100	90
16		5 min	100	96
17		Immediately	100	93
18		45 min	100	90
19		5 min	100	95
20		5 min	100	90

[a] GC yield using an internal standard. [b] The reaction was performed under reflux.

TABLE 3. Reaction of Different Binary Mixtures with PPh_3/DDQ/n-Bu_4NCN[a]

Entry	Binary mixture	Time	Conversion % [b]
1		Immediately	100 5
2		Immediately	100 0
3		Immediately	100 0
4		Immediately	100 5
5		Immediately	100 5
6		Immediately	100 13
7		Immediately	100 0

[a] The stoichiometry of binary mixture/PPh_3/DDQ/n-Bu_4NCN is 1/2/2/2. [b] GC yield using an internal standard.

lides.[10] On continuation of this study, we now report that 1°, 2°, and 3° alcohols, thiols, and trimethysilyl ethers can be efficiently and smoothly converted into their corresponding alkyl cyanides in good to excellent yields using PPh_3/DDQ/n-Bu_4NCN under neutral and mild reaction conditions (Scheme 1).

Because DEAD is expensive, is not easily available, and can be exploded with heat, we first investigated the possibility of its replacement and used DDQ as well as other sources of electron-deficient reagents such as *p*-chloranil, diethylacetylenedicarboxylate (DEACD), TCNE, tetraphenylcyclopentadienone (tetracyclone), and 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD) in conjunction with PPh_3 for this transformation. The conversion of benzyl alcohol to benzyl cyanide with n-Bu_4NCN in the presence of PPh_3, the above-mentioned reagents, and also DEAD was investigated. The results of this study are shown in Table 1.

As is demonstrated in Table 1, the use of PPh_3/DDQ is the most efficient mixed-reagent system for the conversion of benzyl alcohol to benzyl cyanide. Replacement of DDQ by *p*-chloranil or DEAD produces benzyl cyanide in only 7 and 10%, respectively. Other mixed-reagent systems (Table 1, entries 4−7) do not produce any nitrile product.

To optimize the reaction conditions, we first examined the effect of different ratios of ROH/PPh_3/DDQ/n-Bu_4NCN and the solvent and the order of addition for the

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[10] Iranpoor, N.; Firouzabadi, H.; Aghapour, Gh.; Vaez zadeh, A. R. *Tetrahedron* **2002**, *58*, 8689.

conversion of benzyl alcohol to benzyl cyanide. Employing the ratio of 1/2/2/2 in CH_3CN at room temperature gave the best result and produced benzyl cyanide immediately in a quantitative yield. The order of addition is also very important. When the mixture of PPh_3 and DDQ was prepared in acetonitrile, *n*-Bu_4NCN was added to this mixture followed by the addition of the alcohol. We then applied our optimized conditions for the conversion of the structurally different alcohols into their corresponding alkyl cyanides. The results are shown in Table 2. As shown in Table 2, this method is very suitable for the conversion of primary, secondary, tertiary, and benzylic alcohols. Although the capability of DDQ to oxidize benzylic alcohols has been demonstrated,[11] in our reactions, no oxidative product was observed. We also applied this method for the conversion of thiols to their corresponding alkyl cyanides (Table 2, entries 14−16). In these reactions, the corresponding alkyl cyanides were obtained in high yields without the formation of any disulfides through dimerization of thiols. When we applied our method to trimethylsilyl ethers, the reactions furnished their corresponding alkyl cyanides in high yields. (Table 2, entries 17−20).

To see the applicability and limitation of this new method, we studied the possibility of the conversion of alcohols in the presence of some other functional groups in binary mixtures (1:1) using the same stoichiometry of the reagents to substrate as before. The most important point about the selectivity of this reaction is that primary alcohols can be converted to their corresponding alkyl cyanides with excellent selectivity in the presence of secondary and tertiary ones. This reagent also converts alcohols into alkyl cyanides with excellent selectivity in the presence of thiols and silyl ethers. The conversion yields obtained for the selective reactions of different binary mixtures are shown in Table 3.

In conclusion, the present investigation has demonstrated that the use of PPh_3/DDQ/*n*-Bu_4NCN offers a simple, novel, and convenient method for the conversion of wide varieties of alcohols, thiols, and silyl ethers to their corresponding alkyl cyanides. The method shows excellent selectivity not only between different alcohols but also between alcohols, thiols, and trimethylsilyl ethers. Availability, safety, ease in handling of the reagents, high yields, and mildness of the reaction conditions make this method novel for direct conversion of alcohols, thiols, and trimethylsilyl ethers into cyanides.

Experimental Section

Typical Procedure for Conversion of Benzyl Alcohol to Benzyl Cyanide. To a flask containing a stirring mixture of DDQ (2 mmol, 0.454 g) and PPh_3 (2 mmol, 0.524 g) in dry CH_3CN (5 mL) was added *n*-Bu_4NCN (2 mmol, 0.537 g) at room temperature. Benzyl alcohol (1 mmol, 0.1 mL) was then added to this mixture. The green color of the reaction mixture immediately changed to brown. GC analysis showed the immediate completion of the reaction. The solvent was evaporated. Column chromatography of the crude mixture on silica gel using *n*-hexane as an eluent gave benzyl cyanide in 94% yield. The product was identified by the comparison of its physical constants and IR and NMR spectral data with those of an authentic sample.

Typical Procedure for the Competitive Reactions. *n*-Bu_4NCN (2 mmol, 0.537 g) was added to a stirring solution of DDQ (2 mmol, 0.454 g) and PPh_3 (2 mmol, 0.524 g) in dry CH_3CN (4 mL) at room temperature. A mixture of 2-phenylethanol (1 mmol, 0.122 g) and 2-octanol (1 mmol, 0.129 g) in acetonitrile (2 mL) was then added to this mixture. GC analysis of the reaction using *n*-octane as an internal standard showed the immediate completion of the reaction and the formation of 3-phenylpropionitrile and 2-octyl cyanide in 100% and 5% yields, respectively.

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[11] (a) Wang, W.; Li, Y.; Attardo, G. *J. Org. Chem.* **1997**, *62*, 6598. (b) Becker, H. D.; Bjork, A.; Adler, E. *J. Org. Chem.* **1980**, *45*, 1596.